

the transduction of important morphogenetic signals. The genetic and cell biological control of ciliogenesis, however, is poorly understood. Here we show that mutation of the zebrafish *iguana* gene strongly inhibits primary cilia formation. *Iguana* encodes a zinc finger and coiled-coil containing protein, which we have previously implicated in Hedgehog signaling. We now argue that aberrant Hedgehog signaling in *iguana* mutants arises from their lack of primary cilia. Consistent with this, we have found that like in mammals, the 7-pass transmembrane protein Smoothed translocates to primary cilia in cells of the zebrafish embryo in response to Hedgehog activity. Despite the obligatory requirement of *Iguana* for primary ciliogenesis, surprisingly, its loss has a relatively mild effect on the assembly and function of motile cilia. Our findings identify the *Iguana* protein as a novel and critical component of the primary ciliogenic pathway.

doi:[10.1016/j.ydbio.2009.05.372](https://doi.org/10.1016/j.ydbio.2009.05.372)

#### Program/Abstract # 344

##### Dishevelled controls apical docking and planar polarization of basal bodies in ciliated epithelial cells

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The planar cell polarity (PCP) signaling system governs many aspects of polarized cell behavior. Here, we use an *in vivo* model of vertebrate mucociliary epithelial development to show that Dishevelled (Dvl) is essential for the apical positioning of basal bodies. We find that Dvl and Inturned mediate the activation of the Rho GTPase specifically at basal bodies, and that these three proteins together mediate the docking of basal bodies to the apical plasma membrane. Moreover, we find that this docking involves a Dvl-dependent association of basal bodies with membrane-bound vesicles and the vesicle-trafficking protein, Sec8. Once docked, basal bodies again require Dvl and Rho for the planar polarization that underlies directional beating of cilia. These results demonstrate previously undescribed functions for PCP signaling components and suggest that a common signaling apparatus governs both apical docking and planar polarization of basal bodies.

doi:[10.1016/j.ydbio.2009.05.373](https://doi.org/10.1016/j.ydbio.2009.05.373)

#### Program/Abstract # 345

##### PCP signaling: A genome-wide screen for new Rho kinase substrates

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Planar Cell Polarity (PCP) signaling regulates the establishment of polarity within the plane of a tissue, and is required for the

determination of cell fates, the generation of asymmetric, but highly aligned structures (e.g. stereocilia in the human inner ear or fly wing hairs), and the directional migration of cells during convergent extension, a process required for vertebrate gastrulation and neural tube closure. PCP is governed by the non-canonical Fz/PCP pathway, in which activation of a Fz receptor leads to nuclear responses, as well as to cytoskeletal changes mediated by Rho Kinase (Drok). In *Drosophila*, PCP is essential for the alignment of ommatidia in the eye, which requires proper specification of photoreceptor cells, as well as the coordinated movement of groups of photoreceptor cells, thus making it an ideal system to analyze PCP signaling *in vivo*. We performed a genome wide *in vitro* screen to identify new Drok substrates using a phosphorylation induced gel-shift assay. We are currently characterizing candidates using *in vivo* RNAi, mutational analysis, and genetic interaction assays with known PCP and Drok pathway components. One new Rho Kinase substrate we identified is the formin *frl*. Formins are known to regulate actin polymerization dynamics, and the *Xenopus* formin XDAAM was previously shown to be activated by Dishevelled during convergent extension. *Frl* genetically interacts with Drok, and its knock-down causes PCP phenotypes in the eye, suggesting *frl* may be the first *Drosophila* formin identified that is required for PCP signaling.

doi:[10.1016/j.ydbio.2009.05.374](https://doi.org/10.1016/j.ydbio.2009.05.374)

#### Program/Abstract # 346

##### Distinct developmental roles of planar cell polarity proteins vangl1, prickle1, and prickle2 in cortical crescents and primary cilia

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Planar cell polarity (PCP) is manifested as the coordinated, polarized orientation of cells within epithelial sheets, or as directional cell migration and intercalation during convergent extension. Several PCP genes regulate these two developmental processes but their individual roles and interactions are poorly understood. Ciliary mutants display PCP defects, revealing that primary cilia also play a role in PCP. Genetic interaction between Vangl2 and Vangl1 has been observed, but the specific function of Vangl1 in PCP remains uncharacterized. Here, we show that mouse Vangl1 regulates left/right asymmetry in the ventral node, and that it cooperates with Vangl2 to regulate PCP in the vestibular epithelium. In both tissues, VANGL1 protein co-localizes with other PCP proteins in two different subcellular compartments: in apical cortical crescents, a conserved pattern typical of PCP proteins, as well as in a subset of primary cilia. These results confirm that some aspects of PCP signaling are highly conserved from flies to mammals. The presence of PCP proteins in primary cilia suggests a unique vertebrate-specific aspect of PCP signaling, which may explain the requirement for primary cilia in planar polarity.

doi:[10.1016/j.ydbio.2009.05.375](https://doi.org/10.1016/j.ydbio.2009.05.375)